IN THE UNITED STATES DISTRICT COURT FOR THE NORTHERN DISTRICT OF ILLINOIS EASTERN DIVISION

IN RE: ZIMMER NEXGEN KNEE IMPLANT PRODUCTS LIABILITY LITIGATION	)	**MDL NO. 2272**
	)	**Master Docket Case No.: 1:11-cv-05468**
	)	**ALL CASES**
This Document Relates to All Cases	)	
	)	**JUDGE REBECCA PALMEYER**

PLAINTIFFS' TECHNICAL MEMORANDUM ON KNEE ANATOMY, TOTAL KNEE REPLACEMENT AND THE ZIMMER NEXGEN HIGH-FLEXION COMPONENTS AND MIS SURGICAL TECHNIQUE

PREAMBLE

The human knee is a miracle of nature that supports the entire body weight on four small surfaces through a variety of motions essential to everyday life. It is also the joint most susceptible to arthritis among all such joints. With the increases in life expectancy in the 20th Century, people began to suffer pain and disability from knee joint arthritis at historic rates. Knee replacement technology can provide a surgical solution to the pain and restore basic function. Knee replacement designs approved in the 1990's met the goals of reducing pain and restoring function with low failure rates. Despite this success, Zimmer began to tinker with the original design in an effort to replicate the natural knee. Of course, the replacement knees using artificial structures of metal and plastic can in no way replicate the capabilities of the natural knee. Beginning with the Zimmer NexGen Flex knee design in 2001, knee replacement devices and procedures were marketed on the basis of "enhanced" capabilities, "minimally invasive" procedures, and gender specific designs, promising consumers, doctors and patients alike, more movement, shorter hospital stays and better fit than the existing, well functioning and reliable models. In reality however, these enhanced replacement knees did not deliver on any of these promises. Worse, the "flex" design resulted in significantly higher failure rates than their standard knee counterparts. As a result, thousands of knee replacement patients have had more expensive, more dangerous and less effective revision surgery.

Explanation:

There are five figures referenced throughout the paper, which provide mini images to assist in the explanation of some of the technical aspects. Full size images have been attached for the Court's convenience. It's best to view the full size image at the same time as reading the section of the paper where the mini image is referenced. While these images will be helpful, the PSC will present a much more elaborate, animated visual presentation on January 12, 2012 which will form a substantial supplement to this basic paper.

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I. BASIC ANATOMY

From a lay perspective, the knee is a hinge joint where the bottom of the thigh bone and top of the shin bone move in one plane. However, the functional anatomy of this joint is much more complex, as the bones are not directly attached to each other but are held together by rope-like ligaments. Movement is created by the action of muscles and tendons. The joint hinge bears weight directly on its moving surfaces which are made of specialized cartilage.

A. Bones

The knee is composed of three functional bones; the femur (thigh), tibia (shin) and patella (kneecap). The femur is the longest and strongest bone in the body. The lower end of the femur, known as the distal end, forms the upper part of the knee. This distal end has two rounded knob like projections called "condyles", with a groove in between. One condyle is on the medial (inside) of the knee, and the other on the lateral(outside) of the knee. These rounded condyles articulate (move) along the top of the tibia while the back of the patella (kneecap) moves along the groove between the condyles.

The tibia is the main bone in the lower leg. The top of the tibia is relatively flat and is called the "tibial plateau." The articulating areas are also called condyles. The rounded condyles of the femur articulate upon the condyles of the tibia.

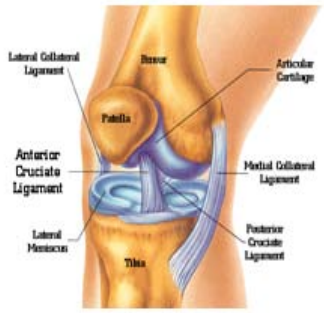

Fig.1 – basic knee anatomy

The patella or kneecap is a mostly flat, oval shaped, bone tapered toward the distal end. The posterior, or back side, of the patella glides in the groove between the condyles of the femur and articulates with the femur.

There is a fourth bone, the smaller bone in the lower leg, called the fibula, which is the attachment for the lateral collateral ligament, but is not directly involved in the movement.

All of the bones of the knee have nerve endings and direct blood supply. The outside of the bone is called cortical bone and is, for purposes of this discussion, solid. The inside is made up of cancellous or trabicular bone which has a lattice-like structure.

B. Articular Cartilage

The articulating surfaces of the knee bones are covered with articular cartilage, which has unique chemical and physical properties that make it very functional as a smooth lubricated joint surface. When healthy, these surfaces create less friction when moving past each other than water on ice. They allow the joint bones to glide easily past each other during knee motion and serve as a protective layer for the bones they cover. Articular cartilage also distributes the weight of the body (load) evenly over the joint, spreading the pressure.

Unlike bone which is nourished by direct blood supply and has nerves, articular cartilage has neither direct blood supply nor nerve endings. Damage to cartilage is not painful. Pain occurs when the articulating cartilage loses its ability to spread the load evenly over the joint, creating pressure points on the bone (think of stepping on a toe with a flat wide shoe heel versus the same weight with a spiked heel). Pain also occurs when the cartilage loses the physical properties that allow bones to glide easily because the joint becomes inflamed.

Cartilage is an elastic connective tissue consisting of a dense matrix of collagen fibers and proteoglycans. The matrix is produced by cells called chrondoblasts, which become embedded in the matrix as chrondocytes. Collagen is organized by the chrondocytes to both stabilize the surface of the cartilage and allow openings in the matrix to absorb fluid, providing nourishment to the cartilage. Proteoglycans are large molecules that both absorb water and release it under the pressure of gravity and muscle contraction. The porosity of the matrix allows water and sugar to flow in and out. The knee joint is surrounded by a joint capsule, and within that capsule fluid from a highly vascular synovial lining nourishes the articular cartilage. Synovial fluid originates from blood plasma that is filtered by the vascular network within the synovium. Synovial fluid transports nutrients, assists in the joint's defense, and lubricates the joint. Sixty-five to 85% of cartilage weight consists of water, which allows for load dependent deformation. Collagen forms 10 to 20% of the weight of the cartilage and provides tensile strength. Proteoglycans form 10 to 20% of the net weight of the cartilage and provide compressive strength as well as maintain the fluid and electrolyte balance in the artiucular cartilage. The remaining 1 to 5 % of weight is made up of the chondrocytes.

The articular cartilage is linked to the underlying bone by a complex geometric interlocking system, much like jigsaw puzzle pieces. Bone and cartilage are not connected in any way other than a mechanical connection. For a real life example, think of the white surface on soup bone (cartilage) before cooking and how it will separate from the bone easily after cooking but with both bone and cartilage intact. Otherwise bone and cartilage are anatomically separate, with separate systems for growth, nutrition and regeneration.

Arthritis develops when the cartilage surface wears away creating increased pressure on the bone and therefore pain. Damage to the surface allows proteoglycans to escape, causing the cartilage to lose its firmness and increase wear. Damage is repaired by fibrous tissue which does not have the same properties as the original tissue. “Arth” means joint. The suffix “osis” means damage. The suffix “itis" means inflammation. In osteo-arthritis, water content rises to ninety percent due to increased permeability and disruption of the matrix, which leads to decreased elasticity and reduction in load bearing capability.

Two other parts of the articulating joint are the menisci. The menisci (“meniscus” singular) are wedge shaped in profile and C shaped when seen from above. The ends of the menisci attach to the intercondylar area of the tibia (between the condyles). The menisci create concavity on the tibial plateau upon which the femoral condyles rest. They also act as shock absorbers, spreading the impact of motion across the joint surfaces.

Knee replacement is the process of replacing the joint surfaces with artificial materials. The replacement is not nearly as good as the original but it redistributes weight and takes away the tissue causing inflammation and thus reduces pain. Replacement requires a mechanical connection between the bones and the implant components, but this bonding is never as good as the natural bonding of cartilage to bone.

II. STRUCTURAL ANATOMY

Joint stability is dependent upon geometry and soft tissues. The soft tissue stabilizers are divided into two types: static (ligaments) and dynamic (muscles and tendons).

A. Ligaments

The knee is completely dependent on ligaments for its structural integrity. The most important ligaments outside of the joint capsule are the patellar ligament, the medial collateral ligament (MCL) and the lateral collateral ligament (LCL). The patellar ligament is in the front (anterior) of the knee joint and forms the distal part of the quadriceps tendon connecting the powerful front quadriceps (thigh) muscles and the lower leg. The primary function of these muscles, ligaments and tendons is to straighten or "extend" the leg. The LCL extends from the lateral (outside) femoral condyle to the lateral (outside) surface of the tibial head. The MCL extends from the end of the medial (inside) fermoral condyle to the medial condyle and upper part of the medial surface of the tibial plateau. It is also firmly attached to the medial meniscus. The MCL and LCL hold the femur and the tibia together, and resist side to side motion.

The main ligaments inside the joint are the posterior cruciate ligament (PCL) and the anterior cruciate ligament (ACL). "Cruciate" means "cross" and these ligaments cross each other like an "X" in the center of the knee. The PCL arises from the back of the tibial plateau between the condyles and passes on the medial side of the ACL to attach to the anterior part of the lateral surface of the medial condyle of the femur. The ACL attaches posterior to (behind) the medial meniscus on the front of the tibial plateau between the condyles and passes above, behind, and lateral to the PCL, where it attaches to the posterior part of the medial side of the lateral femoral condyle.

The ACL and PCL aid in holding the knee together and resist forward and backward sliding of the femur over the tibia.

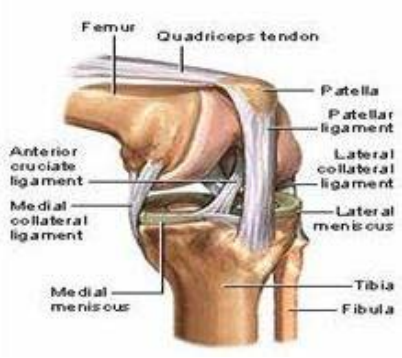

Fig. 2 – Normal flexed knee

B. Muscles and Tendons

The main motions of the knee joint is flexion (bending) and extension (straightening), with limited medial and lateral rotation.

Flexion is produced by group of muscles known as the hamstring muscles. The hamstring muscle generally is attached inner side to tibia and latter side to the fibula.

C. Movement

The knee is a complex joint that is capable of different types of movement, all guided by soft tissues rather than a solid bone structure. When the knee is in alignment, the body's weight is supported through the lower joints, with the knee experiencing the greatest load, followed by the hip and then the ankle. This loading helps explain why osteoarthritis occurs more frequently in the knee than in the hip (a socket joint) or the ankle (a mortise joint), as the risk of developing osteoarthritis is inversely proportional to the stability of a joint.

Movement is based upon the geometry of the knee and the soft tissues, but is most dependent on the soft tissues; ligaments, tendons and muscles.

As stated above, the principle movement of the knee is flexion which is bending the knee, and, extension, which is straightening the knee. Typically, a healthy knee has the potential to bend to about 155 to 160 degrees. One limiting factor on flexion is the girth of the leg, so that the knee may not reach 155 degrees even though it is anatomically able to because the soft tissues of the thigh and calf contact each other before full flexion is reached. The healthy knee can extend typically to a little more than 0 degrees, which is a little beyond straight.

Most normal movements of everyday life such as walking, climbing and descending stairs, getting out of a chair, getting in and out of a car, or stooping generally require only up to 90 degrees of flexion. A modestly active person needs only about 95 degrees of flexion.

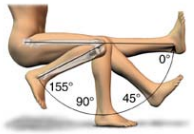

Fig. 3 – Degrees of flexion

Infrequently, activities of daily living require up to 120 degrees of flexion, for example, getting up off the floor, or getting out of a seat where the hip is lower than the knee when seated. Flexion beyond 120 degrees is only required by a limited number of activities such as squatting, certain types of kneeling, and extreme sports activities. Loads created by flexing the knee can be up to 5 times the body weight. The further the knee is flexed while weight bearing, the higher the loads become. Forces on the knee are affected by position (standing versus squatting, for example) and movement. The knee is also subject to direct forces (gravity weight when standing up straight) and rotational forces (when moving and on one foot, the center of gravity is medial to the center of the knee, causing a rotational force.)

III. TOTAL KNEE REPLACEMENT (TKR)

A. Procedure, Components & Materials

When disease or injury disrupt normal knee function causing pain and disability that prevents necessary activities of daily living, the three articulating bone surfaces of the knee may be replaced in what is known as a Total Knee Replacement (TKR), or Total Knee Arthroplasty (TKA). Despite the name, a TKR is not truly a joint replacement, but rather a resurfacing of damaged articular cartilage and bone surfaces. The main goals of the procedure are: (1) to

relieve pain caused by arthritis, (2) to restore range of motion, or the degrees of knee flexion and extension, and (3) to correct any misalignment. Although TKRs are common, with over 500,000 being performed in the U.S. each year, they are still a major surgery, requiring several days of hospital stay and months of rehabilitation. During the procedure, the bone surfaces are cut-to-shape using special guides and tools. The lower end of the femur is covered by a curved, metal femoral component. The top surface of the tibia is covered by a flat, metal tray. Virtually all designs also have a stem or pegs that insert into the center of the tibia. A polyethylene articular surface snap-fits into a tibial tray and the femoral component slides over this surface as the knee bends. Nothing directly connects the femoral component to this articular surface. Finally, the back of the patella is replaced by a dome-shaped, polyethylene component. The MCL and LCL are maintained and continue to hold the knee together. The ACL is always removed. The PCL may be retained or may be removed and replaced with a post on the polyethylene surface.

Fig. 4 – Knee with implanted device

The metallic femoral component and tibial tray are made of chrome cobalt (Cr/Co) or titanium aluminum (Ti/Al), whereas the articular surface and patella are made of polyethylene, a type of plastic. During a TKR, either cemented or cementless fixation can be used to attach the metal components to the bone. For cemented fixation the implants have one surface pre-coated with a thin layer of acrylic bone cement during the manufacturing process. During surgery, a fast-curing bone cement called polymethylmethacylate (PMMA) bonds to the pre-coat on the implant and interdigitates with the lattice structure inside the bone to hold the component in its place. The cement should not be viewed as a "glue" but rather like mortar which infiltrates the latticework and then hardens. While the use of cement assists in fixation, it has certain negative properties including extending the length of the operation, increasing the risk of emboli, and, if revision is ever necessary, requiring the removal of more bone. Cementless fixation involves porous implants, whose surfaces are coated with small metal beads or fibers. The porous metal attracts bone growth directly into the pores on the implant creating a mechanical bond in a process called osseointegration.

B. History of Total Knee Replacement

In the late nineteenth century, Theophilus Gluck designed and implanted the first total knee replacement joint, made of ivory .This model was a true hinge hammered into the bone. The first acrylic hinge replacement was introduced in 1951, and upgraded to metal (Co-Cr) in 1958. These early models of hinge prosthesis often failed, largely due to poor metallurgy and fixation methods that resulted in frequent infections. Design limitations in the early days of total knee replacements included improper sizing as well as fixation, no provision for replacing the patellofemoral joint, and lack of rotational freedom.

Modern condylar and unicompartmenal total knee replacements were developed between 1969 and 1980. The "condylar" implant essentially mimicked the shape of the condyles. These designs were non-hinged, preserved both cruciate ligaments, and used methyl-metacrylate cement, approved by the FDA for general use in 1971. The early designs did not include a patellofemoral joint replacement, did not replace all the condyles and had a small contact area, thereby leading to high rates of loosening of the tibial component. The true condylar knee, where all surfaces of the femoral and tibial plateau are replaced, and which requires less bone resection when compared with earlier hinge prosthesis, was the combined effort of numerous surgeons and design engineers working separately and together, both in the United States and abroad. In 1971 in London, Michael Freeman and Alan Swanson created the first implant to rely solely on component geometry and soft-tissue balance to provide stability. In 1974, Freeman's protégé John Insall, along with Chitranjan Ranawat and Peter Walker, introduced the first total condylar knee. Replacing the patellofemoral joint, became standard practice.

The first cementless condylar total knee replacements took place at Johns Hopkins in 1978, with cementless fixation becoming more widely implemented throughout the early 1980s. By the late 1980s, stem fixation and metal wedges were introduced for revision surgeries. Despite potential advantages of cementless fixation, these component designs remained controversial, and cemented fixation remained the "gold standard".

C. History of Zimmer NexGen

In 1927, Justin Zimmer, a national sales manager for Depuy, an orthopedic splint manufacturer, broke away and started Zimmer Manufacturing Company. Originally a company that manufactured aluminum orthopedic braces, it quickly expanded into the surgical implant business. Today Zimmer designs, develops, manufactures, and markets orthopedic implants as well as fracture products and surgical tools.

In 1995, Zimmer introduced its Next Generation (NexGen) Complete Knee Solution system, with various component configurations as well as surgical guides and tools. Designed largely by John Insall, the system received FDA 510(k) clearance, demonstrating that the device was "substantially equivalent" to predicate devices previously cleared by the FDA. The NexGen TKR was an integrated system combining a femoral component, a tibial component, a plastic articulating surface and a plastic replacement for the posterior surface of the patella. The surgeon had the option to save or remove the posterior cruciate ligament.With the NexGen CR (Cruciate Retaining) implant, the PCL is preserved. In the LPS (Legacy Posterior Stabilized) version the posterior cruciate ligament is sacrificed. The LPS implant includes a raised surface with an internal post on the tibial component that fits into a special notch on the femoral component. The post and notch work together to perform the function of the PCL: preventing the tibia from moving too far backward. The basic system was very successful with a low revision rate. The system was able to achieve flexion up to between 120 and 130 degrees, depending on the patient. Zimmer became the largest US manufacturer of knee replacement

devices. Knee replacement is Zimmer's largest single line of business, with sales from knees alone exceeding $1.7 billion in 2010, amounting to 42% of company revenue. Despite the success of the NexGen and other Zimmer products, the knee replacement manufacturing industry remained highly competitive with at least 4 other major manufacturers.

While the standard NexGen CR (Cruciate Retaining) and NexGen LPS (Legacy Posteror Stabilized or cruciate sacrificing) produced excellent results and sales, the push to increase market share or expand the market to younger more active patients caused sellers to design implants that could arguably provide more function or were more attractive to the consumers, whether the consumer was a patient, a hospital, a health system or a surgeon. The first step in that direction was the NexGen LPS Flex Fixed-Bearing Knee was which got FDA 510k approval in 1999 and was introduced in 2001. The LPS-Flex was designed to allow for a maximum flexion of 155 degrees. The NexGen CR Flex followed in 2003, also allowed up to 155 degrees of flexion.

In 2004, Zimmer launched its Minimally Invasive Solutions (MIS) Quad-Sparing TKR Procedure. Whereas traditional TKR incisions are 8-12 inches, Zimmer's MIS incision is 3-5 inches and avoids cutting a portion of the quadriceps muscles and tendon. The stated goals were less blood loss, less pain, a shorter hospital stay, and shorter rehabilitation. On the negative side, a smaller opening limited the surgeon's view of the operative field, and required some specialized and smaller instruments and components.

In 2006, Zimmer launched Gender Solutions, a femoral component designed specifically for women. Differences between traditional and Gender Solutions Female (GSF) implants include a thinner profile, contoured shape, and a difference angle between the pelvis and the knee to more mimic the general anatomic differences between the female and male knee (other than size).

D. The Advent of Premium Knees

With the introduction of the Insall and other basic knee designs, the market became crowded with knee prostheses that could reliably eliminate pain and restore the ability to perform most daily functions with a low failure rate. The only ways to increase market share was to either expand the patient base of those who receive implants (for example, younger more active patients) or offer TKR with alleged enhancements such as more function, shorter recovery times or prostheses designed to gender specifications. Called in some publications "premium knees", the new designs were more expensive but at the same time more attractive to many patients and surgeons. Zimmer took the lead in this area with 3 different enhancements. The basic NexGen LPS and CR knees were redesigned so they had the potential to flex a full 155 degrees. The minimally invasive surgery, or MIS (Minimally Invasive Solutions), promised a quicker exit from the hospital and quicker recovery. The "Gender Solutions" knee, all of which were flex knees, were redesigns of the standard CR and LPS, but shaped slightly different to mimic the typical anatomical differences between a male and female knee. Patients were promised that

they could recover faster, and engage in more active lifestyles. Women, who were roughly 2/3 of the knee implant market, were told they could get a knee replacement designed just for them.

1. The NexGen High-Flex Knee

Zimmer's NexGen high-flex knees were designed to reach 155 degrees of flexion. The pre-existing standard NexGen knee implants were designed to flex to 120 degrees. The extra flexion is largely achieved through a redesign of the femoral component by expanding the size and thickness of the posterior condyle. This modification requires the removal of more bone. The promise was the knee could achieve the extremes of flexion of a healthy knee. The majority of normal daily activities do not require more than 120 degrees of flexion. For example, climbing stairs requires 90 degrees of flexion, the ability to go from a standing position to a sitting position requires between 90 to 110 degrees. Activities such as squatting, yoga, or kneeling with buttocks on heels may require more than 120 degrees of flexion. The flex concept was first developed in Asia, where squatting, deep kneeling and sitting crossed legged are prominent cultural features.

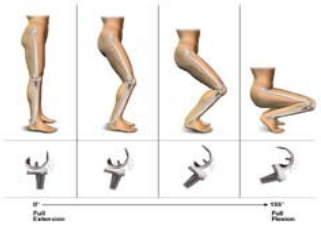

Fig. 5 – Flexed knee device

In the US, Zimmer has aggressively marketed its high-flex versions as specifically designed for younger and more active total knee replacement patients "expecting to maintain an active lifestyle".

2. The "NexGen Minimally Invasive Solutions" (MIS)

Zimmer claims to have revolutionized the TKR industry with its MIS system which modified the tibial component of the knee replacement and certain operative instruments to allow for knee surgery through a much smaller incision. A key component of this MIS system was the NexGen MIS stemmed tibial component which allowed, for the first time in the industry the possibility of performing a minimally invasive TKR. In order to allow for the smaller incision, the device was designed to be assembled inside the patient. The design of the tibial plate was changed so that broad proximal fins engaged the tibia for fixation and its low profile allowed for insertion in a smaller incision. The design had an optional drop down extension which could be used to increase stem length, which was left to the surgeon's discretion. As is typical in the industry, Zimmer provided detailed instructions on surgical technique and took the lead in providing education and training to surgeon who would perform this procedure.

3. The Gender Specific knee replacement (Gender Solutions Female)

Zimmer's launch of the Gender Solutions Female (GSF) femoral components was another industry first. Prior to the GSF, different components were not used for male and female TKR patients.

Zimmer changed the shape of the femoral component to mimic the differences in the shape of the female knee. According to Zimmer, the anterior of the distal end of the female femur is narrower than in the male knee. In order to accommodate this difference, both the lateral and medial condyle heights of the component were altered. Additionally, the trochlear groove angle of the component is increased by thee degrees to allow for better patellar tracking to accommodate the distinct Q-angle difference in the female knee.

All the Gender Solutions components are high-flex designs capable of 155 degrees of flexion.

E. The Selling of the Premium Knee

The cost of premium knees is significantly greater than the standard knees. The standard NexGen CR and LPS femoral components are about $4,000, except for the CR and LPS porous components which are over $5,000. The CR-Flex knees range from $5,970 to $7,390 and the LPS-Flex knees range from $6,090 to $7,390 depending on the coating options. If a surgeon chooses to go with the Gender Solutions knee the cost can be as high as $8,100 for the LPS and CR GSF porous knees. With each premium knee options such as Flex, Gender Solutions and porous coating the price continues to increase. The most expensive femoral component in the NexGen line is the revision system, the LCCK, which is $9,080. This is the only option that Zimmer offers for a revision device.

Once the surgeon chooses to go with the high-flex option they will also need to utilize the high-flex articular surface, which also costs more. The standard CR articular surface costs $1,700 and the CR-flex articular surfaces cost between $1,900 and $2,270. The LPS is slightly more expensive at $1,980 for the standard and the flex between $2,140 and $2,380. The articular surface for the revision device costs $3,010.

The costs of the tibial plates range from about $2,500 to $3,000 depending on the coating options. However, if the MIS is used the cost of the plate is $3,440 and the drop down plug is about $1,060 and if an extension stem is used that costs an additional $1,480. Another MIS option is the trabecular metal technology plate which costs $3,800.

The total cost of one of these devices can be anywhere from about $7,400 for a standard device with no premium options, to approximately $14,280 with all the premium options available. When the device fails and needs to be revised the cost can be as much as $15,090.

IV. THE PROBLEMS WITH THE PREMIUM KNEE

A. Studies Have Repeatedly found no Additional Benefits in Patients with the High-Flex Knee

Several peer reviewed studies have looked at the benefits of high-flex knees compared to standard knees and they repeatedly find that patients with the high-flex knees do not have better ROM than patients with the standard knees. A recent study published in 2010 provided a meta-analysis of these studies, the majority of which involved NexGen knees. It reviewed and analyzed data from 11 studies comparing a total of 561 high-flex knees with 563 standard knee implants.[1] Seven of the trials looked at Posterior Stabilized designs (PS, where PCL is removed) and 4 trials compared the Cruciate Retaining design implants. The analysis revealed that patients in each group, the high-flex and the standard, achieved an average post-operative ROM of 110 degrees. The analysis also revealed no statistical differences in knee ROM, weight-bearing flexion, knee scores and complications among the two groups.

In 2005, a study of 50 patients all receiving the NexGen LPS-Flex in one knee and LPS standard fixed bearing prosthesis in the other knee, found that the mean range of motion, post-operatively, was 135.8 degrees for standard knees and 138.6 for high flex knees. The authors concluded that after a two year follow up, there were no significant differences regarding range of motion or clinical and radiographic parameters, except for posterior femoral condyle offset. This latter finding was determined to be "not clinically relevant".[2]

A 2009 study found similar results when examining 54 patients who received a standard NexGen CR implant in one knee and CR-Flex in the other knee. Post-operatively the mean range of motion with and without weight bearing was 131 degrees and 115 degrees, respectively with the standard prosthesis and 133 degrees and 118 degrees, respectively with the high-flex prosthesis. The authors found no significant difference between the two groups with regard to range of motion or clinical or radiographic parameters.[3] There are several studies that have compared the clinical outcomes of patients who received a NexGen high-flex implant with patients who had the standard knee implants and consistently the high-flex group does not have a better ROM or clinical success.

B. Studies and FDA Reports Indicate Problems of Premature Failure with the NexGen High-Flex Devices.

The longevity of any prosthetic knee implant is limited. Over time, the metal and polyethylene components wear as they roll and slide against each other. However, a typical implant is expected to last beyond 10 years and in a substantial majority of cases 20 years. When loosening or failure occurs within five years, there is no question that the failure is premature. Certainly individual factors such as infection, surgeon error and patients eccentricities can affect implant longevity, but when studies are done that minimize these factors, the blame for early failure clearly falls on the implant design and manufacture.

1) The NexGen LPS Flex Cemented: In 2007, Han reported a high incidence of femoral component loosening with the NexGen LPS-Flex knee. The study looked at 72 LPS-Flex knees that were cemented in 47 patients and found aseptic loosening in 38% at a mean follow up of 32 months. Fifteen knees required revision (21%). Han found that the "loosened" group had a greater mean flexion both functionally and by measurement than the non-loosened group. Han suggested the following mechanism to explain the loosening:

> As the knee flexes beyond 135°, the patella clears the femoral groove and is in contact only with the condyles. Therefore, during deep knee flexion, the distally directed force on the femoral component is resisted not by the bony patella but by the quadriceps muscle, which is elastic and weak in elderly, arthritic patients. Femoral components with intramedullary stems may be appropriate for high-risk patients, but this may in turn produce greater stress shielding and secondary weakening on the bone.[4]

2) The NexGen CR Flex Porous (cementless) Femoral Component: Problems of early loosening with flex implants came to the forefront when an abstract was presented at the 2010 meeting of the American Academy of Orthopedic Surgeons. Two well known joint replacement surgeons from the renowned Rush Medical Center, Richard Berger and Craig Della Valle, reported a high failure rate in the NexGen CR-Flex cementless design. This was significant because Dr. Berger had a long association with Zimmer and had been a proponent of their products. The report stated as follows:

> Two surgeons performed 146 primary TKAs between July and October of 2005. During this period, a cementless [CR]-flex femoral component with a cemented tibial component was used in 120 cases (82%). Of the 120 hybrid knees, 108 (90%) knees had been clinically and radiographically evaluated for evidence of osseointegration. Of these 108 knees, 39 (36%) were radiographically loose, 9 (8.3%) were revised for failed femoral loosening with pain, and one has an impending revision. [T]his cementless CR-flex femoral component has a high incidence of failure of osseointegration; 39 of the 108 cases (36%) were loose. Moreover, 9.3% had a revision or impending revision. This component is still commercially available but should not be used for any patient. Furthermore, this report highlights the

> need for clinical studies prior to new design implementation.

In response to Berger and Della Valle's findings, Zimmer has relied heavily on the Australian Joint Registry. As reported in the business media:

> In a statement, Zimmer said this NexGen CR-Flex Porous Femoral component "has a strong track record of clinical success." The Warsaw, Ind., company also said evidence from an Australian registry and Zimmer surveillance "demonstrates that it is a safe and effective product when used as indicated in the surgical technique." [5]

Although the Australian Registry seems to support Zimmer's claims on its face, a closer examination shows higher failure rates with the flex design. First, while the Zimmer NexGen products do well against most competitors, the critical comparison is the NexGen standard versus the NexGen Flex knees. Second, the average number of years of observed experience is much less for the flex versions. Both the standard CR and LPS have an average of over 5 years of experience while the CR-Flex is 2.4 years and the LPS Flex is 2.8 years (2010). When comparing the same years of experience, at one year, the revision rate for the CR was 0.4 while the CR Flex was 0.6, which means the Flex has a 50% higher failure rate than the standard CR. The 2011 results show that the revision rate for the CR Flex and the LPS Flex are from 30% to 43% higher than the standard models per 100 observed years. Finally, the Australian registry has a relatively low number of reported surgeries. The total number of reported surgeries in the Australian registry for TKR by all manufacturers (269,266) is about one half the number of TKR performed in the U.S. in one year.

Although the U.S. does not have a joint registry, the FDA Maude Reports show significant increases in the adverse event reporting related to these knees. In 2006 there were 4 reports of failure for both the MIS and Flex NexGen devices. By 2008, the number of adverse reports was nine times higher. By 2010, the adverse reports for the Flex devices were up to 101 and 71 for the MIS. Within the first 6 months of 2011, there were already 100 reports of failure relating to flex devices. While these numbers seem low, it is widely known that the voluntary MAUDE reporting system dramatically under reports adverse events and that the real number may be 10 to 20 times the number actually reported. For example, The Australian registry, on which Zimmer relies, reports much higher numbers of implant failures with a smaller population. Although there seems to be a decline in 2011 in the number of adverse event reports for the MIS;[6] it is likely due to fewer doctors attempting this difficult surgery and the 2010 recalls relating to these devices.

Individual physicians have also reported high failure rates in their practice. For example, one center reported to the FDA a 20% failure rate after two years when using the cementless

NexGen flex knees. The author of the report is not revealed under FDA regulations but will be determined during discovery.

C. The Gender Solutions Knee Does Not Provide Better Results

The altered design of the NexGen Gender Solutions line does not provide a better fit for the female knee. Every knee is different despite gender and requires the same cuts to be made to the femur bone to shape it to fit the femoral component. There have been several comparison studies looking at the outcomes of the Gender knee implants compared to their non-gender flex counter parts. A 2010 study involving 85 women who received the LPS-Flex in one knee and the Gender Solutions LPS-Flex in the other knee found no significant clinical benefits between the two groups. The mean range of motion was 125 degrees for the LPS-Flex and 126 for the gender specific LPS-Flex. [7]

Another comparison study involving 138 women who received the CR-Flex in one knee and the Gender Solutions CR-Flex in the other, yielded the same results. The range of motion was 123 and 127 respectively for the two groups. [8] The reality is, when the surgeon makes the bone cuts to the femur and tibia, the anatomical differences between the typical male and female knee are cut off. All the matters clinically is the fit of the components to the bone and each other.

D. Problems with the NexGen MIS Procedure

Minimally invasive procedures gained appeal in the medical community with the advent of laparoscopic and endoscopic procedures where there is no incision at all. Zimmer took a medical term, MIS, which commonly refers to minimally invasive surgery, and made its own trademark with a twist on the acronym – "Minimally Invasive Solutions". There is no true minimally invasive surgical technique for a TKR.

The MIS procedure is a harder surgery by the very nature of performing a TKR in a much smaller area with limited visibility. In an MIS surgery the incision is 3 to 4 inches as compared to a 6 to 12 inch incision required for a normal TKR surgery. Also, the technique of preserving part of the quadriceps muscle blocks the view of the posterior lateral aspect of the knee so that part of the surgery is performed blind.

In 2010 there were two recalls on two different types of NexGen MIS tibial tray plates. In March, Zimmer recalled its MIS trabecular metal technology tibial tray because of a manufacturing defect causing the titanium to disintegrate and break apart from the tray. This recall involved over 800 products. Later that year there was a recall on the MIS stemmed tibial component, specifically, the surgical technique brochure that said the drop down stem was optional. Zimmer warned against not using the drop down stem because they were finding that the tibial plate was prematurely loosening and resulting in revision surgery. This recall affected about 68,384 devices.

Despite the continued problems with the MIS tibial plates and the added difficulty and complications that this technique presents, Zimmer continues to heavily promote the surgery, claiming faster healing time, less blood loss and shorter hospital stays. However, the length of the incision is not a determining factor for blood loss or healing time. If all other variables are equal, a 3 inch incision will heal in the same amount of time as a 12 inch incision. The risks associated with a very difficult partially blind TKR surgery do not outweigh the benefit of a smaller scar.

V. REVISION OF A TOTAL KNEE REPLACEMENT

Patients with loose implants experience an increase in pain and swelling as well as a decrease in knee function, which may result in a limp, stiffness, or instability. Patients who experience these symptoms as a result of premature implant failure must undergo a revision surgery, during which the loose implant is replaced with a new one. Although revision surgeries are a much more serious operation than primary total knee replacements, with a higher risk of failure, there are few viable alternatives.

Revision TKR's are more complex than primary procedures, and take longer to perform, often lasting as long as two to three hours. After removing the implant as well as any underlying cement, the surgeon must compensate for additional bone loss before attaching the new, specialized components.

Most individuals who require a revision surgery have experienced significant bone loss as a combined consequence of whatever disease or injury disrupted normal knee function, bone removal required during primary TKR, and bone erosion resulting from a loose component. Loosening leads to further bone erosion by the following process: uneven wear on an implant creates microscopic debris particles. The body attempts to digest these debris particles, initiating or exacerbating an inflammatory response. During this biological response, bone is also digested in a process called osteolysis. As normal wear on the implant as well as micro-movement of the loose components continues, so does bone erosion and further loosening.

Management of significant bone loss during revision surgeries includes the use of femoral augments, tibial wedges, bone grafts, or cement filler, as well as specialized implants with longer stem extensions to compensate for inadequate bone stock. However, revision surgeries require additional bone removal in order to make the bone surfaces even, as well as to accommodate extra-long stems. Consequently, revision implant systems have less bone surface area to which to spread pressure and loads.

Overall, revision surgeries demand more complicated surgical techniques, require specialized or even custom implants and tools, and carry an increased complication rate, with higher rates of infection and earlier failure than primary total knee replacements. Furthermore, hospital stays tend to be longer and recovery times slower; patients also tend to obtain less overall function. Finally, young patients who require a revision surgery still face the risk of needing a second revision surgery.

ENDNOTES

[1] Shi-xing Lou, M.D. et al., *High Flexion vs. Conventional Prostheses Total Knee Arthroplasty: A Meta-Analysis*, The Journal of Arthroplasty, Vol. 00, No. 0, 2010.
[2] *Kim, Y et al, Range of Motion of Standard and High-Flexion Posterior Stabilized Total Knee Prosthesis, 2005*, Journal of Bone and Joint Surgery, *1470- 1475.*
[3] Kim Y., *et al, Range of Motion of Standard and High-Flexion Posterior Cruciate-Retaining Total Knee Prostheses: A Prospective Randomized Study*, Journal of Bone and Joint Surgery, 2009, 1874-1881.
[4] Han H., *High incidence of loosening of the femoral component in legacy posterior stabilized-flex total knee replacement*, Journal of Bone and Joint Surgery (BR), 2007, 89-B;1457-61.
[5] http://www.advfn.com/news_UPDATE-Surgeons-Warn-Of-Problems-With-Zimmer-Knee Product_41939604.html
[6] Within the first 6 months of 2011 there were 21 reports that identified the device as a MIS as compared to the two previous years there were 71 reports for MIS devices. This seems to indicate a projected decline.
[7] Kim Y., *et al, Comparison of a Standard and a Gender-Specific Posterior Cruciate Substituting High-Flexion Knee Prosthesis: A Prospective, Randomized Short Term Outcome Study*, Journal of Bone and Joint Surgery, 2010, 92:1911-1920.
[8] Kim Y., *et al, Comparison of Standard and Gender-Specific posterior-cruciate-retaining High-Flexion Total Knee Replacements*, Journal of Bone and Joint Surgery (British), 2010, 92-B;639-645.

Respectfully submitted,

PLAINTIFFS' STEERING COMMITTEE

/s/ James Ronca_____
James Ronca, Esq. (SBN 25631)
ANAPOL, SCHWARTZ, WEISS, COHAN, FELDMAN & SMALLEY, PC
1710 Spruce Street
Philadelphia, PA 19103
Tel: (215)735-1130
Fax: (866)735-2792
Email: Jronca@anapolschwartz.com

Timothy Becker
Johnson Becker PLLC
33 South Sixth Street, Suite 4530
Minneapolis, MN 55402
Phone: (612) 333-4662
Fax: (612) 339-8168
Email: tbecker@johnsonbecker.com

Tobias Milrood
Pogust, Braslow and Millrood
Eight Tower Bridge, Suite 1520
161 Washington Street
Conshohocken, PA 19428
Phone: (610) 941-4204
Fax: (610) 941-4245
Email: tmillrood@pbmattorneys.com

Co-Lead Plaintiffs' Counsel

Peter Flowers
Foote Meyers Mielke & Flowers, PC
3 North 2nd Street, Suite 300
Saint Charles, IL 60174
Tel. (630) 232-6333
Email: pjf@foote-meyers.com
Plaintiffs' Liaison Counsel

FIGURE 1- Basic Knee Anatomy

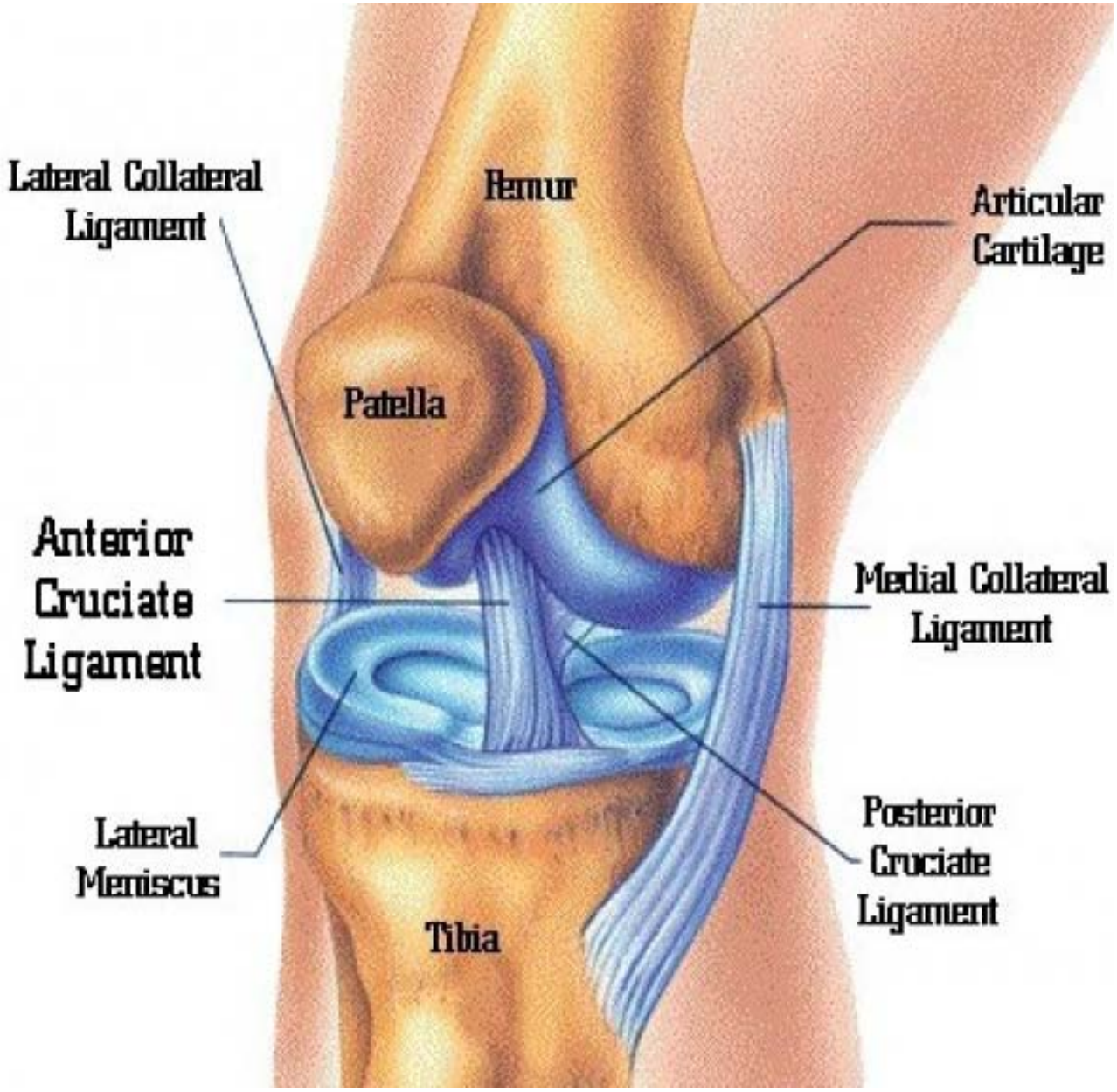

FIGURE 2- Normal Flexed Knee

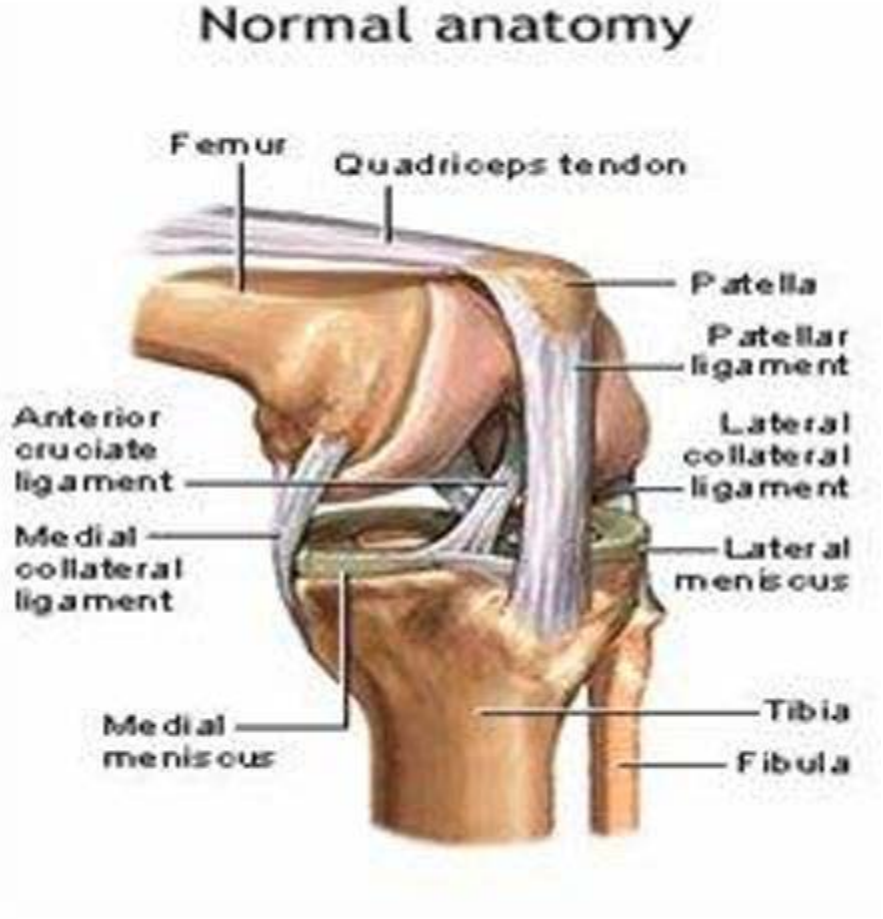

FIGURE 3- Degrees of Flexion

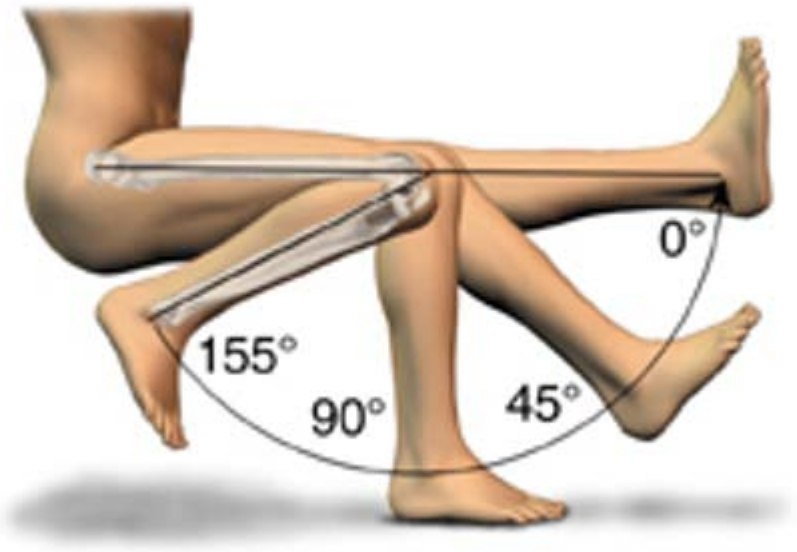

FIGURE 4- Knee with Implanted Device

FIGURE 5- Flexed Knee Device